***Oath/Declaration***

In the present Office Action, the Examiner notes that the declaration submitted by Applicants on November 19, 2001 is defective because the signature of inventor, Gideon Strassmann, is missing. The Examiner has thus required the submission of a new oath or declaration in compliance with 37 CFR §1.67(a).

Applicants respectfully point out that a petition under 37 CFR §1.47(a) was filed in the parent application (Application No. 09/305,989; now U.S. Patent 6,368,597) on January 9, 2001 (copy enclosed), given the refusal of Dr. Gideon Strassmann to sign the Declaration, Petition, and Power of Attorney document. As evidenced by the enclosed Decision According Status under 37 CFR 1.47 (a) dated June 18, 2001, the Office of Petitions granted the petition on June 18, 2001. According to the Decision, Applicants successfully showed "that the non-signing inventor has refused to join in the filing of the parent application. Furthermore, Applicants have established that the non-signing inventor, Mr. Strassmann, received the application papers and refused to sign the declaration." Accordingly, Applicants respectfully submit that the requirement for Gideon Stassmann's signature in the present continuing application, as in the parent application, should be excused, and respectfully request the Examiner to withdraw the objection.

***Rejection of Claims 1-3; 5-8 and 11 Under 35 U.S.C § 112, First Paragraph***

I. The Examiner has rejected claims 1-3; 5-8 and 11 under 35 U.S.C. §112, first paragraph, as "containing subject matter which was not described in the specification in such a way to reasonably convey one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." In particular, the Examiner argues that:

> The claimed invention is drawn to methods of increasing the expression of GLUT4 or a method of increasing insulin sensitivity in a subject by

administering a GDF-8 inhibitor. However, no structural or specific functional characterisitics of such a peptide fragment inhibitors, GDF-8 receptor agonist, dominant negative mutant GDF-8, a non-GDF-8 peptide, antisense, ribozyme inhibitors and an inhibitor that is derived from the Pro-GDF-8 domain is provided.

Applicants respectfully traverse the foregoing rejection and maintain that the Applicants' patent specification describes the claimed invention in sufficient detail to show that Applicants were in possession of the claimed invention at the time of filing.

The fundamental factual inquiry in a written description rejection is whether the claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed. The subject matter of the claim ***need not be described literally*** (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the written description requirement. MPEP 2163.02. Rather, the inquiry into whether the written description requirement is met must be determined on a case-by-case basis and is a question of fact. *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). Moreover, the Examiner has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *In re Wertheim* 541 F.2d 257, 265, 191 USPQ 90, 98 (CCPA 1976); *Ex parte Sorenson*, 3 USPQ2d 1462, 1463 (BPAI 1987). MPEP 2163.04.

The instant specification provides specific functional characteristics unique to several GDF-8 inhibitors. In particular, Applicants define inhibition of GDF-8 activity as any inhibition of activity which is mediated by GDF-8, including, for example, inhibition of fibroblast differentiation to adipocytes and the modulation of the production of muscle-specific enzymes (see page 6, line 3-7 of the specification). In addition, specific examples of several GDF-8 inhibitors are described in the specification at page 5, lines 10-15, including peptides, dominant-negative protein mutants, antibodies or fragments thereof, ribozymes, antisense oligonucleotides or other small molecules which specifically inhibit the action of GDF-8 while, preferably, leaving intact the activity of TGF-β, activin or other members of the TGF-β superfamily. Other GDF-8 inhibitors which can be employed in the methods of the invention are well known in the art and are incorporated by reference in the present specification, such as the inhibitors described in

U.S. Serial No. 60/116,639, entitled "Growth Differentiation Factors and Uses Therefore," (see page 5, line 18-23 of the specification).

The Court in *Regents of the University of California v. Eli Lilly & Co*, 119 F. 3d 1559 (Fed. Cir. 1997), held that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by, structure, formula, or chemical name of the claimed subject matter sufficient to distinguish it from other materials." As applied to the present case, this standard is fully satisfied as discussed above, the present specification describes the structure and function of several particular GDF-8 inhibitor constructs. From this description, it would be more than apparent to one of ordinary skill that Applicants had possession of the claimed invention at the time of filing. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-3; 5-8 and 11 under U.S.C. § 112, first paragraph.

II. The Examiner has also rejected claims 1-3, 5-8 and 11 under 35 U.S.C. §112, first paragraph as "containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." In particular, the Examiner argues that the specification does not reasonably provide enablement for peptide fragment inhibitors, GDF-8 receptor agonists, GDF-8 dominant negative mutants, non-GDF-8 peptides and antisense and ribozyme inhibitors." The Examiner bases the rejection on the premis that Applicants have not provided any biochemical data, such as molecular weight and amino acid composition of the peptide inhibitors." The Examiner further argues that:

> [t]he applicant also does not disclose what biochemical features a non-GDF-8 peptide inhibitor encompasses. The specification neither teaches the GDF-8 receptor nor making a receptor agonist; claiming a biochemical molecule by a particular name given to the protein fails to distinctly claim what the protein is and what the composition is made of. The specification does not teach how to make and use the claimed inhibitors; without such guidance the applicant is inviting the artisan to engage in undue experimentation.

Applicants respectfully traverse the foregoing rejection and maintain that the present specification provides a more than sufficient disclosure to have enabled the ordinarily skilled artisan to have made and used GDF-8 inhibitors as claimed without undue burden.

Specifically, Applicants' specification teaches how to produce a variety of GDF-8 inhibitors (page 9, line 1, through page 16, line 19 of the specification), how to test their efficacy both *in vivo* (page 31, lines 14-30 of the specification) and *in vitro* (page 16, line 20, through page 17, line 7 of the specification), and how to administer them to subjects (page 18, line 6, through page 24, line 2 of the specification).

The Examiner asserts that Applicants have not disclosed "any biochemical data, such as molecular weight and amino acid composition, of the peptide inhibitors." Applicants respectfully disagree. From the outset, such data is not needed to enable the scope of the present claims. Rather, the proper inquiry is whether the specification provides sufficient guidance to have made and used GDF-8 inhibitors as claimed. As described in detail above, Applicants specification does indeed provide such guidance by way of describing several known GDF-8 inhibitors as well as methods for making and identifying other inhibitors.

Moreover, the particular structural features of several GDF-8 peptide inhibitors are indeed also taught in applicant's specification (see *e.g.*, page 11, lines 17-20 of the specification). For example, Applicants describe a peptide inhibitor comprising, *i.e.*, the pro-domain of GDF-8 (see *e.g.*, page 5 of the specification); as well as several other particular peptide inhibitors as described in U.S. Serial No. 60/116,639, entitled "Growth Differentiation Factor Inhibitors and Uses Therefor"(see *e.g.*, page 5, lines 20-23 of the specification).

In view of the foregoing, Applicants respectfully submit that the ordinarily skilled artisan, following a careful reading of the above-described teachings from Applicants' specification, could have made and used a variety of GDF-8 inhibitors, such as peptide inhibitors, GDF-8 receptor antagonists, dominant negative mutants of GDF-8, and GDF-8 antisense and ribozyme inhibitors, to increase expression of GLUT4 in a subject, to

increase insulin sensitivity and glucose uptake by cells in a subject, and to treat diabetes in a subject, all as instantly claimed. Furthermore, In view of the foregoing teachings in the Applicants' specification, and the general knowledge available in the art at the time of the invention, Applicants respectfully submit that any experimentation that may be required to practice the claimed methods would be routine, not undue experimentation. Accordingly, it is respectfully submitted that the pending claims are fully enabled by the disclosure, and the Examiner is requested to withdraw this section 112, first paragraph rejection.

***Double Patenting***

The Examiner has rejected claims 4, 9, 10 under 35 U.S.C. §101 as "claiming the same invention as that of claims 1-7 of prior U.S. Patent No. 6,368,597."

Applicants have cancelled claims 4, 9 and 10 so that they are no longer co-extensive in scope. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 101 be reconsidered and withdrawn.

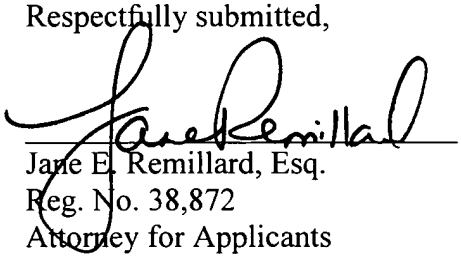
The Examiner has rejected claims 1-3, 5-8 and 11 under the judicially created doctrine of obviousness-type double patenting as "being unpatentable over claim 1-7 of U.S. Patent No. 6,368,597." In particular, the Examiner argues that "although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims are drawn to treatment methods with an antibody inhibitor."

Applicants will file a terminal disclaimer in compliance with 37 CFR 1.321(c) upon the indication of allowable subject matter, if appropriate. Accordingly, Applicants respectfully request that the rejection under judicially created doctrine of obviousness-type double patenting be reconsidered and withdrawn.

## CONCLUSION

Reconsideration and allowance of all the pending claims is respectfully requested. If a telephone conversation with Applicants' Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,



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